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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1636	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/849,781	SNYDER ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/9/11*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) ____ is/are allowed.

6)☒ Claim(s) *1-11,141,164,169,173,174,177,181-186,188,193-195,199 and 200* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/9/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-16,93-101,106,107,112-133,138-159,162,164,165,167,169,171,173-175,177,181-186,188,193-195,199 and 200.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 12-16, 93-101, 106, 107, 112-133, 138-140, 142-159, 162, 165, 167, 171, 175 and 196-197 .

DETAILED ACTION

Status of Claims

Claims 1-16, 93-101, 106, 107, 112-133, 138-159, 162, 164-165, 167, 169, 171, 173-175, 177, 181-186, 188 and 193-195 and 199-200 are pending.

Claims 12-16, 93-101, 106, 107, 112-133, 138-140, 142-159, 162, 165, 167, 171, 175 and 196-197 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species, there being no allowable generic or linking claim.

Claims 17-92, 102-105, 108-111, 134-137, 160-161, 163, 166, 168, 170, 172, 176, 178-180, 187, 189-192 and 196-198 have been cancelled.

Claims 1-11, 141, 164, 169, 173, 174, 177, 181-186, 188, 193-195 and 199-200 are under consideration in this Office Action.

Withdrawn Objection and Rejections

In view of applicants' arguments and Schweitzer's declaration filed on 5/9/11 the 35 USC 112, first paragraph rejections have been withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102/§ 103

Claims 1-11, 141, 181-186, 188, 193-195 and new claims 199-200 are rejected under 35 U.S.C. 103(a) as being obvious over Uetz et al (Nature, 2/10/2000) for reasons of record as reiterated below.

Uetz et al, throughout the reference, teach a protein array representing yeast genome encoded proteins (see Abstract of the reference). The reference teaches fusing roughly 6000 potential ORFs (genes) from yeast genome (which comprises approximately 6000 genes) as determined completion of the yeast genome sequencing (see page 623, left col., 1st paragraph. and page 624, left col., 2nd paragraph). Uetz teaches the yeast proteins were expressed in 96-well assay plates (page 624, left col., bottom of 2nd paragraph), which reads on a solid support of the addressable array of claim 1 because each well of the plates would have defined (or addressable positions). The reference also teach each of the protein encoded by a gene is expressed individually in individual wells of the plates as shown in Figure 1 of the reference (page 624), which reads on each protein being at a different position on a solid support of claim 1, for example. The claimed kinase present in the array

would have been inherent to the yeast array taught by Uetz since yeast inherently contain kinase in its structure or would have been obvious to determine given the identified genome of yeast as taught by Uetz. Uetz et al do not specify that their arrays comprise 61 kinases, however, as the arrays disclosed by Uetz et al include all of the approximately 6,000 genes of the Saccharomyces cerevisiae genome, the protein array disclosed by Uetz et al inherently comprises all of the kinases from yeast and therefore meets the limitation of being an array that comprises 61 kinases from yeast. The yeast protein array disclosed by Uetz et al does not comprise proteins arrayed at the densities specified in the claims. It is of note that the array provided in Example 1 of the instant description is a 10x14 array with 1.4 mm wells and a 1.8 mm pitch (pages 32-33), i.e. a density of 30.86 wells/cm2. The instant application acknowledges that fabrication of arrays with submicron feature sizes is known in the art and that protein chip technology is readily scalable (instant description, page 37 lines 29-34). [The same is previously known as disclosed by each of Humphrey-Smith and Sosnowski et al]. Therefore, the construction of high-density protein arrays and the standard technical features of said arrays were previously known in the art.

> Where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same as is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. See In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972); In re Best 195 USPQ 430 (CCPA 1977).

Claim 200 is obvious over the disclosure of Uetz of a kinas as that claimed hence its function to phosphorylate Ser/Thr and Tyr would inherent to the prior art teachings of the same compound. This is evidenced from the instant disclosure (published application 20030207467) at e.g., [0125]:

> The yeast genome has been sequenced and contains approximately 6200 open reading frames greater than 100 codons in length; 122 of these are predicted to encode protein kinases. Twenty-four of these protein kinase genes have not been studied previously.sup.8. Except for two histidine protein kinases, all of the yeast protein kinases are members of the Ser/Thr family; tyrosine kinase family members do not exist although seven protein kinases that phosphorylate serine/threonine and tyrosine have been reported.sup.8.

Response to Arguments

Applicants argue that the large scale assay of Uetz involves an array at which each position on the array contains a pool of "living transformants" that express unpurified mixtures

containing two different recombinant proteins (corresponding to proteins endogenously expressed by the host cell) and most of the 6,000 other proteins such as, protein kinases, that are constitutively expressed by the host cell. Uetz teach a transformed yeast host cell array expressed on 96 well plates that is useful for analyzing protein-protein interactions in vivo in yeast cells using a two hybrid screen. In view of the teaching of Uetz, a person of ordinary skill in the art would not have had a reason to modify the teaching of Uetz to arrive at the claimed array. The passing reference in Uetz to arrays containing purified proteins is unaccompanied by any disclosure or guidance relating to the type, number, activity, or density of the "purified" proteins that "may be envisioned" on this alternatively formatted array. Most significantly, the disclosure of Uetz does not enable arrays containing arrayed purified active proteins. Therefore, even if a person of ordinary skill in the art were motivated to modify the teaching of Uetz, they would not have reasonably expected to be able to successfully make and use the claimed positionally addressable protein arrays.

In reply, in considering disclosure of a reference, it is proper to take into account not only specific teachings of the

reference but also "inferences" which one skilled in the art would reasonably be expected to draw therefrom. In re Preda 159 USPQ 342. A reference is therefore evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. **In re Bozek, 163 USPQ 545 (CCPA 1969).** Uetz teaches more than a passing reference. Uetz teaches that the use of purified proteins, being one of types of protein array, is known in the art and refers to the prior art, Martzen et al (ref. 7). Thus, Uetz discloses purified protein containing the same kinase from yeast. Even assuming that Uetz does not disclose (but Uetz does) a purified kinase as argued however, the unpurified ORF of the yeast containing kinase would be the same as the claimed purified one. A purified kinase obtained from the same source as yeast merely further characterizes the known kinase present in the yeast. And applicants' use of the word "comprising" does not preclude the other elements present in the kinase contain in the ORF region of the yeast. As applicants stated in their REMARKS:

> Kinases and functional kinase domains from yeast, mammals and Drosophila were a well characterized group of proteins that were generally known, understood to be well conserved in structure and function, easily identified, and readily prepared and assayed by those of ordinary skill in the art are known.

It is well settled in the art that where substance having medicinal properties is produced, it becomes an immediate consideration to prepare substances in as pure a form as possible. Claim for known substance which differs from prior art only in degree, as for example in purity, is not patentable. See Ex parte Steelmand and Kelly, 140 USPQ 189. When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d 1385 (2007).

Similarly the claim array of purified kinase is no more than the predictable use of Uetz elements according to their established functions.

Claims 1-11, 141, 181-186, 188, 193-195 and 199-200 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon (WO 95/35505) in view of Felder et al (USP 6458533) or Lafferty (USP 6972183).

Shalon discloses at e.g., page 12, lines 3-9:

> A microarray as an array of regions having a density of discrete regions of at least about 100/cm2, and preferably at least about 1000/cm2. The regions in a microarray have typical dimensions, e.g., diameters, in the range of between about 10-250 um, and are separated from other regions in the array by about the same distance.

Shalon discloses at e.g., page 30, line 30 up to page 32, line 15:

> Sheets of plastic-backed nitrocellulose where each microarray could contain, for example, 100 DNA fragments representing all known mutations of a given gene. The region of interest from each of the DNA samples from 96 patients could be amplified, labeled, and hybridized to the 96 individual arrays with each assay performed in 100 microliters of hybridization solution…… In addition to the genetic applications listed above, arrays of… enzymes…(were prepared].

Shalon discloses an array of enzymes and not kinase as claimed. However, Feder discloses:

> Feder discloses at Example 18:
>
> Kinases are enzymes that attach a phosphate to proteins. Many have been shown to stimulate normal and neoplastic cell growth. Hence, compounds that inhibit specific kinases (but not all kinases) can be used to test whether the kinases are involved in pathology and, if so, to serve as starting points for pharmaceutical development… Each kinase has substrates that are partially identified, as short peptides that contain a tyrosine. Some of the kinase specificities overlap so that different kinases may phosphorylate some peptides equally but others preferentially. For the five kinases, 36 peptide substrates are selected that show a spectrum of specific and overlapping specificities.

Lafferty discloses at e.g., col. 31, lines 41-49 the conventionality of an array containing substrate-enzymes such as kinase.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use in the array of Shalon the enzyme kinase as taught by Feder. Feder teaches that kinase have been shown to stimulate normal and neoplastic cell growth. To use the kinase in the array of Shalon would lead one having ordinary skill in the art in determining the kinase in the array responsible for neoplastic or normal cell growth. Furthermore, as taught by Lafferty an array containing a kinase is known in the art. [See also applicants' admission in the response at page 17, of the 12/19/2006 REMARKS. Applicant states: compositions ***utilizing well-known and well-characterized classes of proteins***, as in the presently claimed invention].

Response to Arguments

Applicants argue that Shalon in one paragraph at the end of the written description section makes the sweeping generalization that "[i]n addition to the genetic applications listed above, arrays of whole cells, peptides, enzymes,

antibodies, antigens, receptors, ligands, phospholipids, polymers, drug cogener preparations or chemical substances can be fabricated by the means described in this invention." Shalon at page 31, line 32 to page 32, line 1. Shalon do not disclose arrays containing a single purified active protein, let alone a group of purified active proteins such as, protein kinases having kinase activity. Significantly, Shalon provide no disclosure that enables the manufacture and use of, for example an "enzyme" array. As clarified in the Office Action, the Examiner relies on Felder and Lafferty "for its disclosure of purified kinase, as claimed, not that it has to teach purifying the kinase prior to immobilization." Office Action at page 30. The Example in Felder cited by the Examiner indicates that kinases are enzymes and discloses the prophetic screening of plates containing peptide substrates with solutions containing proposed known kinases. Felder, Example 18, at cols. 33-34. Significantly, Felder do not disclose or enable arrays containing arrayed purified active kinases. Lafferty disclose arrays containing libraries of clones that express recombinant proteins, among which are listed enzymes, including kinases. See, e.g., Lafferty Field of the Invention Section and col. 4, lines 12-22. Lafferty also disclose that the recombinant enzymes produced by clones identified in the disclosed screens "can be

recovered." Lafferty at col. 18, lines 39-49. Significantly, Felder, like Shalon and Lafferty do not disclose or enable arrays containing arrayed purified active kinases. In view of the teaching of Shalon, Felder and Lafferty, a person of ordinary skill in the art would have no reason to modify the teaching of Shalon to arrive at the claimed positionally addressable arrays. In addition, even if, arguendo, a person of ordinary skill in the art had reason to modify the teaching of Shalon, they would not have predictably arrived at the claimed array. Moreover, as discussed above, the collective disclosure and teaching of Shalon, Felder, and Lafferty do not enable arrays containing arrayed purified active kinases and at best, refer to an array containing enzymes in passing without any guidance as to how such arrays would be prepared or the nature or characteristics of the proteins that would be arrayed.

In reply, applicants' arguments that the Felder reference does not teach how the array is prepared are not commensurate in scope with the claims. The instant claims are drawn to compound, purified kinase from yeast positioned on an array. Shalon, as recognized by applicants above, only mentions in passing arrays. However, this “passing remarks” or inferential teachings suffice the findings of obviousness. As stated above in considering disclosure of a reference, it is proper to take into account not

only specific teachings of the reference but also "inferences" which one skilled in the art would reasonably be expected to draw therefrom. In re Preda 159 USPQ 342.

Applicants cannot attack the references individually when the rejection is based on combination of references. Felder and Lafferty are employed for its disclosure of purified kinase, as claimed, not that it has to teach purifying the kinase prior to immobilization. Shalon teaches ORF containing kinase on an array but does not expressly teach, albeit implicitly, the purified kinase hence, the application of the secondary references Felder and Lafferty that renders the claim prima facie obvious. It would be within one having ordinary skill in the art at the time the invention was made to position a known compound as kinase into an array, as taught by Shalon. There is nothing new and unobvious in mere positioning a known compound in e.g., array, when in nature these kinases are inherently arrayed or attached to e.g., a membrane, which would read on a substrate of an array.

Claim 200 is rejected under the combined teachings of Shalon in view of Felder et al or Lafferty as the claim function of the kinase to phosphorylate Ser/Thr and tyr is inherent to the prior art teachings of the same compound. This is evidenced

from the instant disclosure (published application 20030207467) at e.g., [0125]:

> The yeast genome has been sequenced and contains approximately 6200 open reading frames greater than 100 codons in length; 122 of these are predicted to encode protein kinases. Twenty-four of these protein kinase genes have not been studied previously.sup.8. Except for two histidine protein kinases, all of the yeast protein kinases are members of the Ser/Thr family; tyrosine kinase family members do not exist although seven protein kinases that phosphorylate serine/threonine and tyrosine have been reported.sup.8.

Claims 1-11, 141, 181-186, 188, 193-195 and new claims 199-200 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Meyers et al (US 20090324608).

For claims 1-11, 141, 181-186, 188, 193-195 and new claims 199-200; Meyers teaches at e.g., [0395] an "isolated" or "purified" polypeptide or protein substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. In [0046], Meyers discloses human or non-human animal, e.g., an experimental animal. Meyers discloses at e.g., [0697] an array that includes a substrate having a plurality of addresses. At least one address of the plurality includes a

capture probe that binds specifically to a 53070, 15985, 26583, 21953, m32404, 14089, or 23436 molecule (e.g., a 53070, 15985, 26583, 21953, m32404, 14089, or 23436 nucleic acid or a 53070, 15985, 26583, 21953, m32404, 14089, or 23436 polypeptide). The array can have a density of at least than 10, 50, 100, 200, 500, 1,000, 2,000, or 10,000 or more addresses/cm2, and ranges between. In a preferred embodiment, the plurality of addresses includes at least 10, 100, 500, 1,000, 5,000, 10,000, 50,000 addresses. In a preferred embodiment, the plurality of addresses includes equal to or less than 10, 100, 500, 1,000, 5,000, 10,000, or 50,000 addresses. The substrate can be a two-dimensional substrate such as a glass slide. Addresses in addition to address of the plurality can be disposed on the array.

Meyers teaches at [0143] "protein kinase" includes a protein or polypeptide that is capable of modulating its own phosphorylation state or the phosphorylation state of another protein or polypeptide. Protein kinases can have a specificity for (i.e., a specificity to phosphorylate) serine/threonine residues, tyrosine residues, or both serine/threonine and tyrosine residues. Meyers discloses at e.g., [0691] a computer medium (reads on the claim solid support) having a plurality of digitally encoded data records. Each data record includes a

value representing the level of expression of 53070, 15985, 26583, 21953, m32404, 14089, or 23436 in a sample, and a descriptor of the sample. The descriptor of the sample can be an identifier of the sample or other genes on an array.

Accordingly, Meyers anticipates all the elements of the claim array. The claim array is obvious since Meyers also teaches that the kinase can be positioned on a computer medium which would read on the broad claim solid support. Furthermore, applicants' used of the word "comprising" does not preclude the presence of other components present in the prior art formulation. It has been long held that the use of the term "comprising' leaves a claim open for inclusion of materials or steps other than those recited in the claims". Ex parte Davis, 80 USPQ 448.

Claims 1-11, 141, 181-186, 188, 193-195 and new claims 199-200 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kapeller et al(US 20040048305)(if necessary with Shalon (WO 95/35505)).

For clms. 1-11, 141, 181-186, 188, 193-195 and new claims 199-200; Kapeller et al teaches throughout the patent e.g., [0311] a two dimensional array having a plurality of addresses,

each address of the plurality being positionally distinguishable from each other address of the plurality, and each address of the plurality having a unique capture probe, e.g., peptide sequence; contacted with a 14171 protein kinase, preferably purified, polypeptide, Kapeller discloses at e.g., [0212] the target gene product or the test substance is anchored onto a solid phase. The target gene product/test compound complexes anchored on the solid phase can be detected at the end of the reaction. Preferably, the target gene product can be anchored onto a solid surface, and the test compound, (which is not anchored), can be labeled, either directly or indirectly, with detectable labels discussed herein. Kapeller teaches at e.g., [0269] high density arrays containing hundreds or thousands of oligonucleotides probes. Kapeller teaches at e.g., [0041] a protein kinase includes a protein or polypeptide that is capable of modulating its own phosphorylation state or the phosphorylation state of a different protein or polypeptide. Protein kinases can have a specificity for (i.e., a specificity to phosphorylate) serine/threonine residues, tyrosine residues, or both serine/threonine and tyrosine residues, e.g., the dual-specificity protein kinases. As referred to herein, protein kinases, preferably include a catalytic domain of about 200-400 amino acid residues in length, preferably about 200-300 amino

acid residues in length, or more preferably about 250-300 amino acid residues in length, which includes preferably 5-20, more preferably 5-15, or most preferably 11 highly conserved motifs or subdomains separated by sequences of amino acids with reduced or minimal conservation. Specificity of a protein kinase for phosphorylation of either tyrosine or serine/threonine can be predicted by the sequence of two of the subdomains (VIb and VIII) in which different residues are conserved in each.

Accordingly, Kapeller anticipates the claim array as all the elements of the claim array are taught by Kapeller. Furthermore, the claim density as being the no. of substance/per cm2 density would be obvious per the teachings of Kapeller or would be obvious to determine as evidenced by the teachings of Shalon.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1636